NATIONAL CANCER INSTITUTE
NCI Alliance for Nanotechnology in Cancer

Nanotechnology Heads to the Clinic

The NCI Alliance for Nanotechnology in Cancer makes 7 awards to accelerate the application of nanotechnology to change the way we detect, treat and prevent cancer.

As the 20th century was coming to a close, the National Cancer Institute (NCI) began a program of funding the development and application of "radically new technologies" that had the potential to create the 21st century tools that would transform how physicians detect, treat and prevent cancer. Out of the first five Unconventional Innovations Program (UIP) awards that the NCI made in 1999, one went to James Baker Jr., M.D., a physician and researcher at the University of Michigan who had the opportunistic idea of using a nanometer-diameter, spherical polymer—a dendrimer nanoparticle—to target a tumor with both the means to detect and treat it simultaneously.

Six years later, Dr. Baker and his collaborators at the University of Michigan Nanotechnology Institute for Medicine and Biological Sciences have indeed developed nanoparticles—many different ones, in fact—that data show are capable of detecting and treating cancer at the same time. If all goes well, the first of these multifunctional nanoscale devices should begin clinical trials in human cancer patients within the next year.

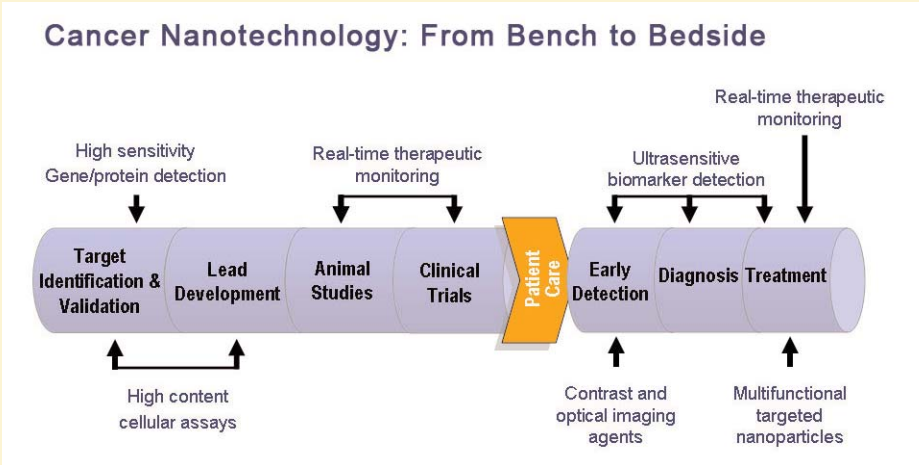
Better yet, one of Baker's colleagues at Michigan and another early UIP awardee, Raoul Kopelman, Ph.D., is developing a different multifunctional nanoparticle that also shows promise as a cancer detection and treatment tool. So, too, is Paras Prasad, Ph.D., a former postdoctoral fellow in Dr. Kopelman's laboratory who has his own successful nanotechnology development program at the State University of New York in Buffalo. Other UIP alumni, including Gregory Lanza, M.D., and his Washington University in St. Louis colleague Samuel Wickline, M.D., and Raymond Sze, Ph.D., and his collaborators at the University of Washington have also developed multifunctional nanoparticles that are nearing clinical trials.

The successes to date of these and other early practitioners of cancer nanotechnology now fuel the next step in the effort to revolutionize cancer detection, treatment and prevention—the focused development of nanotechnology-enabled products for cancer. And the NCI is once again ready to catalyze progress in the field, this time with a major initiative that is not only focused on moving promising research from the laboratory to the clinic, but is also creating the networked, multidisciplinary research teams that the field of cancer nanotechnology must have to drive the field forward as rapidly as possible.

On October 3, 2005, the NCI established seven Centers of Cancer Nanotechnology Excellence (CCNE), awarding a total of $26.3 million for the first of what are expected to be five-year efforts. The CCNEs are multi-institutional hubs that will take a team-based, multidisciplinary approach to focus on integrating nanotechnology into basic and applied cancer research. With this focus, the Centers will be driven to provide new solutions for the diagnosis and treatment of cancer.

"NCI has supported the application of nanotechnology to cancer through a variety of programs and interactions with the scientific community for more than seven years, and we're very gratified that our activities are helping to advance a pipeline of new product opportunities," noted NCI Deputy Director Anna Barker, Ph.D. "But now, for the first time ever, we are seeing multidisciplinary teams comprised of basic and clinical researchers at world-class institutions, all networked together to focus on the key cancer nanotech opportunities."

Dr. Wickline adds, "It's always difficult when you're doing science to develop large multidisciplinary teams, particularly in academia, and maintain the continuity that's required to solve large problems like cancer. This new



CCNE effort is an attempt to get those teams established and to provide the infrastructure that will support them in academia, and I think that is a very forward-looking program and one that will go a long way towards helping solve these problems."

MOVING THE ALLIANCE FORWARD

The newly established CCNEs, just one component of the NCI Alliance for Nanotechnology in Cancer, will serve as hubs to develop and apply nanotechnology and nanoscience solutions to the diagnosis and treatment of cancer. The goals of the CCNE network are to design and test nanomaterials and nanodevices and to translate their use into clinical research, resulting ultimately in the introduction of novel diagnostic tools and techniques to combat cancer processes. The CCNEs will bridge gaps in the development pipeline from materials discovery to testing in clinical trials.

"What we're so excited about in being designated as one of the seven Centers," said Robert Langer, Ph.D., who will be co-director of a CCNE established at the Massachusetts Institute of Technology (MIT) and Harvard University, "is that we will now be able to push all the interesting chemistry and materials science work we've done in our individual laboratories into the clinic, into human trials, and hopefully have a significant impact on cancer."

By balancing structured, milestone-driven directives with investigator-initiated research, these Centers will bring together the interdisciplinary teams from existing NCI-funded laboratories with engineering and materials science groups that have traditionally been funded by other Federal agencies, and provide the infrastructure necessary to develop and translate nanotechnology advances to the clinic. Perhaps more importantly, the multidisciplinary teams at each of the seven CCNEs will be networked with one another through the NCI's Cancer Bioinformatics Grid (caBIG). This nationwide network of local networks will enable rapid data sharing and collaboration that will accelerate the pace of product approval, commercialization, and delivery to cancer patients.

Each of the seven CCNEs, for example, is linked to a regional, NCI-funded Comprehensive Cancer Center and one or more Specialized Programs of Research Excellence (SPOREs). In addition, each of the seven includes both biomedical

MEET THE CENTERS OF CANCER NANOTECHNOLOGY EXCELLENCE

Over the coming months, you will read more about the researchers whose work will drive the efforts of the seven CCNEs. Some of these groups may already be familiar to you from stories that have appeared here on Nano.Cancer.Gov, while others bring new talents and expertise to the NCI's research family. For now, here are brief summaries of what each CCNE plans to accomplish over the next five years.

Carolina Center of Cancer Nanotechnology Excellence

The major thrust of this Center, a collaboration between the University of North Carolina and the Lineberger Comprehensive Cancer Center, is to design and fabricate novel and innovative, multifunctional nanodevices and then test their *in vivo* performance using sophisticated mouse models of human cancer. In addition, this Center will use breakthrough nanodevice fabrication technology to develop nanoscale tools for research and detection applications. In addition to general oncology applications, this CCNE will focus on leukemia; lymphoma; myeloma; and brain, breast, colon, and lung cancers.

The deliverables expected from this CCNE include:

- Smart nanoparticles for cancer therapy and imaging
- Carbon nanotube x-ray devices for in vivo cancer detection and treatment
- Targeted magnetic nanoparticles for brain tumor imaging and therapy
- Chemically patterned nanoscale surfaces for capturing tumor cells
- Nanofluidic devices for rapid, single-cell analysis of tumor cell signaling and migration

Rudolph Juliano, Ph.D. is the principal investigator for this Center.

Center of Nanotechnology for Treatment, Understanding, and Monitoring of Cancer (NANO-TUMOR)

NANO-TUMOR is a collaborative effort involving the University of California, San Diego (UCSD), Moores UCSD Cancer Center, UC-Santa Barbara, UC-Riverside, the Burnham Institute, market research organization NanoBioNexus, and five corporate partners: General Electric Company, Honeywell, Nanogen, Irvine Sensors Corporation, and Enterprise Partners Venture Capital.

The focus of this team will be to develop smart multifunctional nanoplatforms capable of targeting tumors and delivering large payloads of therapeutics and nanosensors to the tumor environment. In addition to general oncology applications, this CCNE will focus on breast cancer and leukemia.

Specific projects of this CCNE include development of:

- Tumor-homing peptide-nanoparticle complexes
- Porous nanoparticles for drug and sensor delivery
- Computational methods for monitoring tumor progression and response using data from nanoparticle-delivered sensors
- Enzyme-sensitive nanoparticle coatings to increase tumor-targeting capabilities of smart nanoparticle platforms

The principal investigator for this CCNE is Sadik Esener, Ph.D., of UCSD.

Emory-Georgia Tech Nanotechnology Center for Personalized and Predictive Oncology

This collaboration between Emory University's Winship Cancer Institute, the Georgia Institute of Technology, and Nanoplex Technologies will focus on the development of bioconjugated nanoparticles for cancer molecular imaging, molecular profiling, and personalized cancer therapy. In addition to general oncology applications, this CCNE will focus on breast, prostate, renal, colon, and bone cancers.

In particular, this CCNE, together with partners at the American Cancer Society and the U.S. Centers for Disease Control and Prevention (CDC) and with additional funding from

researchers and investigators from engineering and physical science departments. All seven have advanced biocomputing capabilities and have forged partnerships with colleagues in the not-for-profit community and/or private sector.

"For many of us, working as part of such interdisciplinary teams is both new and tremendously exciting," said Rudolph Juliano, Ph.D., who will head the CCNE based at the University of North Carolina. "We spent a great deal of time assembling our team, developing our plans for what we would do as a Center, and now we're all looking forward to pushing ahead with projects that can really make a difference in how we detect and treat cancer."

CANCER NANOTECHNOLOGY: PHASE 2 BEGINS

The NCI Alliance for Nanotechnology in Cancer, guided by the NCI's Cancer Nanotechnology Plan, is a $144.3 million, five-year initiative for nanotechnology in cancer research. The Alliance encompasses four major program components:

- **Centers of Cancer Nanotechnology Excellence (CCNEs)** will fund seven hubs over 5 years to develop and apply nanotechnology and nanoscience solutions to the diagnosis and treatment of cancer. These awards were announced on October 3, 2005. Funding for the first year of this program will total $26.3 million.

- **Cancer Nanotechnology Platform Partnerships** are tightly focused programs designed to develop the technologies to underpin new products in six key programmatic areas: molecular imaging and early detection, *in vivo* imaging, reporters of efficacy (e.g., real-time assessment of treatment), multifunctional therapeutics, prevention and control, and research enablers (opening new pathways for research). These 12, five-year awards, with first-year funding totaling $7 million dollars, will be announced this month.

- **The Nanotechnology Characterization Laboratory (NCL)**, established at NCI's Frederick, Md., facility earlier this year, performs analytical tests to guide the research community, support regulatory decisions, and help identify and monitor environmental, health and safety ramifications of nanotech applications. The NCL

the Georgia Research Alliance and Georgia Cancer Coalition, will tackle projects that include the development of:

- Tumor-targeted infrared quantum dots with both optical and magnetic imaging capabilities
- Smart nanoparticle probes for intracellular drug delivery and gene expression imaging
- Antibody-conjugated quantum dots to detect and quantify human breast cancer biomarkers
- Nanoparticle tags for tracking multiple biomarkers in biological specimens using surface-enhanced Raman spectroscopy
- Nanoparticles for delivering therapeutics directly to bone metastases

Shuming Nie, Ph.D., who holds a joint appointment at both Emory University and Georgia Tech, both in Atlanta, and Jonathan Simons, M.D., of Emory University, are the principal investigators for the CCNE.

MIT-Harvard Center of Cancer Nanotechnology Excellence

Organized and administered by the Massachusetts Institute of Technology (MIT) Center for Cancer Research, this Center will be a collaboration among MIT, Harvard University, Harvard Medical School, Massachusetts General Hospital, and Brigham and Women's Hospital. It will focus on developing a diversified portfolio of nanoscale devices for targeted delivery of cancer therapies, diagnostics, non-invasive imaging, and molecular sensing. In addition to general oncology applications, this CCNE will focus on prostate, brain, lung, ovarian, and colon cancers.

Examples of projects that this CCNE will undertake include the development of:

- Targeted nanoparticles for treating prostate cancer
- Polymer nanoparticles and quantum dots for siRNA delivery
- Next-generation magnetic nanoparticles for multimodal, non-invasive tumor imaging
- Implantable, biodegradable microelectromechanical systems (MEMS), also known as lab-on-a-chip devices, for *in vivo* molecular sensing of tumor-associated biomolecules
- Low-toxicity nanocrystal quantum dots for biomedical sensing

In addition to drawing on the scientific and technological expertise of its investigators, this CCNE will use available facilities for toxicology testing and the extensive mouse models of cancer collection at the collaborating institutions. This CCNE has two principal investigators: Robert Langer, Ph.D. of MIT, and Ralph Weissleder, M.D., Ph.D., of Harvard University and the Massachusetts General Hospital.

Nanomaterials for Cancer Diagnostics and Therapeutics

This CCNE represents a strongly integrated partnership between Northwestern University's International Institute for Nanotechnology and the Robert H. Lurie Comprehensive Cancer Center of Northwestern University. This highly multidisciplinary group of nano-scientists, engineers, cancer biologist, and clinicians will use nanotechnology to develop a range of tools with use in clinical oncology using a variety of nanoscale materials and devices. In addition to general oncology applications, this CCNE will focus on ovarian, colon, breast, and prostate cancers and lymphoma.

The six research projects of this CCNE aim to develop:

- Bio-barcodes to detect ovarian cancer markers
- A new class of drugs that will inhibit or reduce metastasis
- Bioactivated nanoprobes for molecular imaging of cancer
- Targeted, multifunctional nanoparticles for drug and radiopharmaceutical delivery
- Nanocomposites for imaging prostate cancer cells and treatment of advanced prostate cancer
- Self-assembling supramolecular nanostructures that deliver chemotherapy agents directly to breast and other cancer tumors

The principal investigator for this CCNE is Chad Mirkin, Ph.D., of Northwestern University in Evanston, Illinois.

recently completed its first year of operation and is actively characterizing nanoparticles for academic and commercial researchers through a rigorous set of analytical protocols. The NCL works in concert with the National Institute of Standards and Technology (NIST) and the U.S. Food and Drug Administration (FDA). For more information, please visit http://ncl.cancer.gov.

- **Multidisciplinary research training and team development:** The application of nanotechnology to cancer challenges requires cross-disciplinary training in biological and physical sciences. The Alliance will support training and career development initiatives to establish integrated teams of cancer researchers, through mechanisms such as the NIH National Research Service Awards for Senior Fellows and the NIH National Research Service Awards for Postdoctoral Fellows. Applications are now being accepted for training awards (http://grants.nih.gov/grants/guide/rfa-files/RFA-CA-06-010.html). In addition, through NCI's collaboration with the National Science Foundation, $12.8 million in grants were awarded last month to four institutions over the next five years for U.S. science and engineering doctoral students to focus on interdisciplinary nanoscience and technology research with applications to cancer (http://www.cancer.gov/newscenter/pressreleases/NCINSFIGERT).

With the announcement of the CCNE awards, the NCI in a sense is ending the first phase of the era of cancer nanotechnology. That phase, which began in 1999 with the first nanotechnology-oriented awards from the UIP program, established the proofs of principle that nanotechnology could indeed provide critically needed new tools for and approaches to detecting cancer at its earliest stage, treating it more effectively and with fewer side effects, and even preventing nascent cancers from developing in the first place.

Based on the exciting results of those pioneering studies, the NCI committed itself to what has been a two-plus year effort to determine how best to realize the promise that cancer nanotechnology has for making dramatic progress toward the goal of eliminating suffering and death due to cancer. Over that time, the NCI's Office of Technology and Industrial Relations (OTIR) solicited input from a broad cross-section of the cancer research and clinical oncology community to first develop its Cancer Nanotechnology Plan. At the same time, the NCI was holding meetings and symposia around the country that were designed to bring together researchers from fields that do not often have the opportunity to discuss areas of mutual interest, and to catalyze the team-building that has led to the creation of these seven CCNEs.

"These seven CCNEs, together with the Platform Partnerships, the Nanotechnology Characterization Laboratory, and our joint efforts with the NSF to train future researchers, represent the vanguard of the NCI's efforts to turn the promise of cancer nanotechnology into real detection tools and real therapies for cancer," said Gregory Downing, D.O., Ph.D., who heads the OTIR. "But what's perhaps even more encouraging is that throughout the process of developing the Cancer Nanotechnology Plan, creating the Alliance, and now funding these powerful groups of investigators, we've seen that the science of nanotechnology and the study of cancer are both at a stage that the combination of the two will almost certainly translate into benefits for patients."

—Joe Alper

Nanosystems Biology Cancer Center (NSBCC)

The NSBCC establishes a collaborative team comprising investigators from the California Institute of Technology (Caltech), the Institute for Systems Biology, UCLA's Geffen School of Medicine, and the Jonsson Comprehensive Cancer Center. The focus of this effort will be to develop and validate tools for the early detection and stratification of cancer through rapid and quantitative measurements of panels of serum and tissue-based biomarkers, and then to use those tools to evaluate the efficacy of various cancer therapies. In addition to general oncology applications, this CCNE will focus on prostate and ovarian cancers, glioblastoma and melanoma.

During the course of the projects that this CCNE will conduct, investigators will develop:

- Molecular imaging and targeting probes using "click" chemistry
- Integrated nanoelectronics/microfluidics chips for multi-parameter diagnostic and measurement tools capable of detecting and quantifying trace biomolecules involved in cancer
- Chip-based tools for isolating rare circulating immune system cells as a means of evaluating the efficacy of immune-based cancer therapies
- Identification of organ-specific, serum-based biomarkers for the detection and stratification of various cancers through blood analysis
- Methods for manufacturing low-cost nanofluidic diagnostic chip-based devices

The principal investigator for the CCNE is James Heath, Ph.D., of Caltech.

Siteman Center of Cancer Nanotechnology Excellence at Washington University

This collaboration between Washington University in St. Louis; the University of Illinois, Urbana-Champaign; the Alvin Siteman Cancer Center; and several private sector start-up companies including, Kereos and Stereotaxis, and multinational companies such as Philips Medical Systems, will concentrate on developing nanoparticles for *in vivo* imaging and drug delivery, and new imaging and characterization tools for characterizing the interactions of nanoscale materials with living cells. In addition to general oncology applications, this CCNE will focus on breast cancer and melanoma.

Projects conducted by this Center's collaborators will include the development of:

- Magnetic nanoparticles that can target multiple tumors for early detection and therapy of cancer
- Nanoparticle-based contrast agent for ultrasound imaging and therapy of tumors
- Bioinformatics tools to create a database for modeling the behavior of targeted nanoparticles in the body
- Novel nanoscale sensors for rapidly screening potential anticancer drugs in single cells

The principal investigator of this CCNE is Samuel Wickline, M.D. of Washington University.